CLAIMS

What is claimed is:

1. Isolated and purified Cyr61, and biologically active fragments, variants, analogs, homologs, and derivatives thereof.

2. An isolated and purified polypeptide having an amino acid sequence as set forth in SEQ ID NO: 4, and fragments, variants, homologs, analogs, and derivatives thereof.

3. The polypeptide according to claim 2 wherein said polypeptide is immunogenic.

4. A polypeptide according to claim 2 wherein said polypeptide is covalently modified.

5. A polypeptide according to claim 4 wherein said covalent modification comprises the covalent attachment of polyethylene glycol.

6. The polypeptide of claim 4 wherein said modification is a fusion with all or part of a different polypeptide.

7. An antibody that specifically binds to a polypeptide according to claim 1.

8. An antibody according to claim 7 wherein said antibody is a monoclonal antibody.

9. A pharmaceutical composition comprising a biologically effective amount of the polypeptide according to claim 1 and a pharmaceutically acceptable adjuvant, diluent, or carrier.

10. A purified and isolated polynucleotide encoding Cyr61.

11. A polynucleotide according to claim 10 wherein said Cyr61 is human Cyr61, and fragments, variants, homologs, analogs, and derivatives thereof.

12. A purified and isolated polynucleotide encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO: 4, and fragments, variants, homologs, analogs, and derivatives thereof.

13. A purified and isolated polynucleotide according to claim 12 wherein said polypeptide encodes a subsequence of the amino acid sequence set forth in SEQ ID NO: 4.

14. A purified and isolated polynucleotide having the sequence set forth in SEQ ID NO: 3.

15. A purified and isolated polynucleotide that hybridizes under stringent conditions to a polynucleotide according to claim 10.

16. A vector comprising a polynucleotide according to claim 10.

17. A host cell transformed or transfected with a polynucleotide according to claim 10.

18. A method of making a Cyr61 polypeptide, comprising the steps of:
(a) Culturing a host cell according to claim 15 under suitable nutrient conditions; and
(b) purifying said polypeptide from said host cell or from a growth medium of said host cell.

19. A method of purifying human Cyr61 comprising the steps of:
(a) obtaining a biomaterial containing human Cyr61;
(b) exposing said biomaterial to a Cyr61-specific biomolecule selected from the group consisting of anti-Cyr61 antibodies and $\alpha_v\beta_3$ integrin;
(c) specifically binding said human Cyr61 to said Cyr61-specific biomolecule; and
(c) eluting said human Cyr61, thereby purifying said human Cyr61.

20. The method according to claim 19 wherein said source comprises human cells.

21. The method according to claim 19 wherein said human Cyr61-specific biomolecule is an anti-human Cyr61 antibody.

22. A method of screening for a modulator of angiogenesis comprising the steps of:
(a) contacting a first biological sample capable of undergoing angiogenesis with a biologically effective amount of an ECM signalling molecule-related biomaterial and a suspected modulator;
(b) separately contacting a second biological sample with a biologically effective amount of an ECM signalling molecule-related biomaterial, thereby providing a control;
(c) measuring the level of angiogenesis resulting from step (a) and from step (b); and
(d) comparing the levels of angiogenesis measured in step (c), whereby a modulator of angiogenesis is identified by its ability to alter the level of angiogenesis when compared to the control of step (b).

23. The method according to claim 22 wherein said modulator is an inhibitor of angiogenesis and further wherein said inhibitor is identified by its ability to decrease said level of angiogenesis when compared to the control of step (b).

24. The method according to claim 22 wherein said ECM signalling molecule is Cyr61, and fragments, variants, homologs, analogs, and derivatives thereof.

25. A method of screening for a modulator of angiogenesis comprising the steps of:

(a) preparing a first implant comprising Cyr61 and a second implant comprising Cyr61 and a suspected modulator of Cyr61;
(b) implanting said first implant in a first cornea of a test animal and said second implant in a second cornea of said test animal;
(c) measuring the development of blood vessels in said first and second corneas; and
(d) comparing the levels of blood vessel development measured in step (c), whereby a modulator of angiogenesis is identified by its ability to alter the level of blood vessel development in said first cornea when compared to the blood vessel development in said second cornea.

26. A method of screening for a modulator of chondrogenesis comprising the steps of:

(a) contacting a first biological sample capable of undergoing chondrogenesis with a biologically effective amount of an ECM signalling molecule-related biomaterial and a suspected modulator;
(b) separately contacting a second biological sample capable of undergoing chondrogenesis with a biologically effective amount of an ECM signalling molecule-related biomaterial, thereby providing a control;
(c) measuring the level of chondrogenesis resulting from step (a) and from step (b); and
(d) comparing the levels of chondrogenesis measured in step (c), whereby a modulator of chondrogenesis is identified by its ability to alter the level of chondrogenesis when compared to the control of step (b).

27. The method according to claim 26 wherein said modulator is an inhibitor of chondrogenesis and further wherein said inhibitor is identified by its ability to decrease said level of chondrogenesis when compared to the control of step (b).

28. The method according to claim 26 wherein said ECM signalling molecule-related biomaterial is selected from the group consisting of a human Cyr61, a human Cyr61 fragment, a human Cyr61 analog, a human Cyr61 derivative,

an antibody specifically recognizing human Cyr61, an inhibitor peptide, mannose-6-phosphate, heparin, and tenascin.

29. A method of screening for a modulator of oncogenesis comprising the steps of:

(a) inducing a first tumor and a second tumor;

(b) administering a biologically effective amount of an ECM signalling molecule-related biomaterial and a suspected modulator to said first tumor;

(c) separately administering a biologically effective amount of an ECM signalling molecule-related biomaterial to said second tumor, thereby providing a control;

(d) measuring the level of oncogenesis resulting from step (b) and from step (c); and

(e) comparing the levels of oncogenesis measured in step (d), whereby a modulator of oncogenesis is identified by its ability to alter the level of oncogenesis when compared to the control of step (c).

30. The method according to claim 29 wherein said modulator is an inhibitor of oncogenesis and further wherein said inhibitor is identified by its ability to decrease said level of oncogenesis when compared to the control of step (b).

31. A method for treating a solid tumor comprising the step of delivering a therapeutically effective amount of a Cyr61 inhibitor to an individual, thereby inhibiting the neovascularization of said tumor.

32. The method according to claim 31 wherein said inhibitor is selected from the group consisting of inhibitor peptides and cytotoxins.

33. The method according to claim 31 wherein said inhibitor is a cytotoxin attached to Cyr61.

34. A method of screening for a modulator of cell adhesion comprising the steps of:

(a) preparing a surface compatible with cell adherence;

(b) separately placing first and second biological samples, each sample capable of undergoing cell adhesion, on said surface;

(c) contacting a first biological sample with a suspected modulator and a biologically effective amount of an ECM signalling molecule-related biomaterial selected from the group consisting of a human Cyr61, a human Cyr61 fragment, a human Cyr61 analog, and a human Cyr61 derivative;

(d) separately contacting a second biological sample with a biologically effective amount of an ECM signalling molecule-related biomaterial selected from the group consisting of a human Cyr61, a human Cyr61

fragment, a human Cyr61 analog, and a human Cyr61 derivative, thereby providing a control;
(e) measuring the level of cell adhesion resulting from step (c) and from step (d); and
(f) comparing the levels of cell adhesion measured in step (e), whereby a modulator of cell adhesion is identified by its ability to alter the level of cell adhesion when compared to the control of step (d).

35. A method of screening for a modulator of cell migration comprising the steps of:
(a) forming a gel matrix comprising Cyr61 and a suspected modulator of cell migration;
(b) preparing a control gel matrix comprising Cyr61;
(c) seeding endothelial cells capable of undergoing cell migration onto the gel matrix of step (a) and the control gel matrix of step (b);
(d) incubating said endothelial cells;
(e) measuring the levels of cell migration by inspecting the interior of said gel matrix and said control gel matrix for cells;
(f) comparing the levels of cell migration measured in step (e), whereby a modulator of cell migration is identified by its ability to alter the level of cell migration in the gel matrix when compared to the level of cell migration in the control gel matrix.

36. The method according to claim 35 wherein said endothelial cells are human cells.

37. The method according to claim 35 wherein said matrix is selected from the group consisting of Matrigel, collagen, and fibrin.

38. The method according to claim 35 wherein said inspecting step comprises microscopic examination.

39. An *in vitro* method of screening for cell migration comprising the steps of:
(a) forming a first gelatinized filter and a second gelatinized filter, each filter having two sides;
(b) contacting a first side of each said filter with endothelial cells capable of undergoing cell migration, thereby adhering said cells to each said filter;
(c) applying an ECM signalling molecule and a suspected modulator of cell migration to a second side of said first gelatinized filter and an ECM signalling molecule to a second side of said second gelatinized filter;
(d) incubating each said filter;
(e) detecting cells on said second side of each said filter; and

(f) comparing the presence of cells on said second side of said first gelatinized filter with the presence of cells on said second side of said second gelatinized filter, whereby a modulator of cell migration is identified by its ability to alter the level of cell migration measured on said first gelatinized filter when compared to the cell migration measured on said second gelatinized filter.

40. The method according to claim 39 wherein said endothelial cells are human microvascular endothelial cells.

41. The method according to claim 39 wherein said ECM signalling molecule is human Cyr61.

42. The method according to claim 39 further comprising the step of placing each said filter in a Boyden chamber.

43. An *in vivo* method of screening for a modulator of cell migration comprising the steps of:

(a) removing a first central portion of a first biocompatible sponge and a second central portion of a second biocompatible sponge;

(b) applying an ECM signalling molecule and a suspected modulator to said first central portion and an ECM signalling molecule to said second central portion;

(c) reassociating said first central portion with said first biocompatible sponge and said second central portion with said second biocompatible sponge;

(d) attaching a first filter to a first side of said first biocompatible sponge and a second filter to a second side of said first biocompatible sponge;

(e) attaching a third filter to a first side of said second biocompatible sponge and a fourth filter to a second side of said second biocompatible sponge;

(f) implanting each of said biocompatible sponges, each biocompatible sponge comprising said central portion and said filters, in a test animal;

(e) removing each said sponge following a period of incubation;

(f) measuring the cells found within each of said biocompatible sponges; and

(g) comparing the presence of cells in said first biocompatible sponge with the presence of cells in said second biocompatible sponge, whereby a modulator of cell migration is identified by its ability to alter the level of cell migration measured using said first biocompatible sponge when compared to the cell migration measured using said second biocompatible sponge.

44. The method according to claim 43 wherein said ECM signalling molecule is human Cyr61.

45. The method according to claim 43 wherein said ECM signalling molecule is associated with Hydron.

46. The method according to claim 43 further comprising the step of providing a radiolabel to said test animal prior to removing said first and second biocompatible sponges and wherein said detecting step comprises the detection of said radiolabel in said first and second biocompatible sponges.

47. A method for modulating hemostasis comprising the step of administering an ECM signalling molecule in a pharmaceutically acceptable adjuvant, diluent or carrier.

48. The method according to claim 47 wherein said ECM signalling molecule is human Cyr61.

49. A method of inducing wound healing in a tissue comprising contacting wounded tissue with an angiogenically effective amount of Cyr61.

50. A method of inducing wound healing in a tissue comprising the steps of:
(a) introducing a nucleic acid comprising a control expression sequence operably linked to an ECM signalling molecule into the cells of a wounded tissue; and
(b) controlling the expression of said coding region, thereby inducing wound healing.

51. The method according to claim 50 wherein said ECM signalling molecule is human Cyr61.

52. The method according to claim 50 wherein said nucleic acid comprises a vector selected from the group consisting of a Herpesvirus, an Adenovirus, an Adeno-associated Virus, a Cytomegalovirus, a Baculovirus, a retrovirus, and a Vaccinia Virus, and wherein said vector comprises an ECM signalling molecule coding region.

53. The method according to claim 50 wherein said wounded tissue is selected from the group consisting of skin tissue and lung epithelial tissue.

54. A method of promoting organ regeneration comprising the step of administering a biologically effective quantity of Cyr61 to an animal.

55. A method of improving tissue grafting comprising the step of administering to an animal a quantity of Cyr61 effective in improving the rate of neovascularization of a tissue graft.

56. A method for promoting bone implantation comprising the step of applying a biologically effective amount of an ECM signalling molecule to a bone implant, thereby promoting bone implantation.

57. A method for promoting prosthesis implantation comprising the steps of:
(a) applying a biologically effective amount of an ECM signalling molecule to a biocompatible wrap such as a biodegradable gauze; and
(b) contacting the wrap with a prosthesis; and
(c) implanting said prosthesis, thereby promoting prosthesis implantation.

58. A method of screening for a modulator of cell proliferation comprising the steps of:
(a) contacting a first biological sample capable of undergoing cell proliferation with a suspected modulator and a biologically effective amount of an ECM signalling molecule-related biomaterial selected from the group consisting of a human Cyr61, a human Cyr61 fragment, a human Cyr61 analog, and a human Cyr61 derivative;
(b) separately contacting a second biological sample with a biologically effective amount of an ECM signalling molecule-related biomaterial selected from the group consisting of a human Cyr61, a human Cyr61 fragment, a human Cyr61 analog, and a human Cyr61 derivative, thereby providing a control;
(c) incubating said first and second biological samples;
(d) measuring the level of cell proliferation resulting from step (c); and
(e) comparing the levels of cell proliferation measured in step (d), whereby a modulator of cell proliferation is identified by its ability to alter the level of cell adhesion when compared to the control of step (b).

59. A method for expanding a population of undifferentiated hematopoietic stem cells in culture, comprising the steps of:
(a) obtaining hematopoietic stem cells from a donor; and
(b) culturing said cells under suitable nutrient conditions in the presence of a biologically effective amount of Cyr61.

60. A method of screening for a mitogen comprising the steps of:
(a) plating cells capable of undergoing cell proliferation;
(b) contacting a first portion of said cells with a solution comprising Cyr61 and a suspected mitogen;

(c) contacting a second portion of said cells with a solution comprising Cyr61, thereby providing a control;
(c) incubating said cells;
(d) detecting the growth of said first portion of cells and said second portion of said cells; and
(e) comparing growth of said first and second portions of cells, whereby a mitogen is identified by its ability to induce greater growth in said first portion of cells when compared to the growth of said second portion of cells.

61. The method according to claim 60 wherein said cells are selected from the group consisting of endothelial cells and fibroblast cells.

62. The method according to claim 60 further comprising contacting said first and second portions of said cells with a nucleic acid label and detecting the presence of said nucleic acid label in said cells.

63. The method according to claim 62 wherein said nucleic acid label is [^{3}H]-thymidine.

64. A kit comprising a polypeptide according to claim 2.